REPLY FILED UNDER EXPEDITED PROCEDURE PURSUANT TO 37 C.F.R. § 1.116

Please cancel claims 58-60, 69-71, 79-81, 90-92, and 97 without prejudice and without disclaimer of the subject matter contained therein.

REMARKS

Upon entry of this amendment, claims 40, 54, 61-65, 72-75, 82-86, 93-96, and 98-101 will be pending in the application. Claims 40, 55, 63, 74, 76, 84, 95, and 99 have been amended herein. Claims 58-60, 69-71, 79-81, 90-92, and 97 are canceled herein without prejudice and without disclaimer of the subject matter contained therein. Claims 40, 63, 74, 84, 95, and 99 have been amended to clarify that the claimed polypeptide is immunologically identifiable by antibodies that react specifically with the protein encoded by SEQ ID NO:3 or with the polypeptide expressed from the nucleotide sequence of SEQ ID NO:2, as supported by the specification, for example, at page 14, lines 21-30. No new matter has been introduced by way of this amendment.

Formal drawings have been submitted to the Drawing Review Branch.

Applicants note with appreciation the withdrawal of rejections as noted in the Office Action. Applicants also note with appreciation consideration of the Supplemental Information Disclosure Statement submitted with the prior response.

I. Claims 61-62, 74, 75, 82-86, 95, 96, and 98-101 satisfy 35 U.S.C. § 112, second paragraph.

Claims 58-62, 74, 75, 79-86, and 95-101 are rejected for alleged indefiniteness under 35 U.S.C. § 112, second paragraph. Preliminarily, Applicants note that claims 58-60, 79-81, and 97 have been canceled herein without prejudice or disclaimer to the subject matter

contained therein. Applicants disagree with the rejection for the reasons of record. Nonetheless, in order to advance prosecution of the application, Applicants have amended the claims to overcome the rejection.

Claims 55, 57-59, 76, and 78-80 are rejected for alleged indefiniteness in recitation of the term "derivative." Applicants note that claims 57 and 78 were canceled by prior response. Applicants have canceled claims 58, 59, 79, and 80 herein and have amended claims 55 and 76 to omit reference to "derivative." Accordingly, Applicants request withdrawal of the rejection.

Claims 58 and 79 also are rejected for alleged indefiniteness in the recitation of the phrase "immunologically identifiable with." Applicants have canceled those claims without prejudice herein and request withdrawal of the rejection.

Claims 59 and 80 are rejected for allegedly being indefinite for reciting the phrase "which do not substantially affect." Applicants submit that this rejection has been mooted by cancellation of claims 59 and 80.

Applicants submit that the claims as amended herein satisfy the requirements of 35 U.S.C. § 112, second paragraph. Accordingly, Applicants request withdrawal of the rejection.

II. The specification provides adequate written descriptive support of claims 95 and 96 as amended.

Claims 95 and 96 are rejected under 35 U.S.C. § 112, first paragraph for alleged lack of adequate written description. Applicants disagree for the reasons of record. Nonetheless, to advance prosecution of the application, Applicants have amended claim 95 to overcome

the rejection. Claim 95 has been amended to recite a polypeptide that is immunologically identifiable by antibodies that react specifically with a polypeptide of SEQ ID NO:3. Applicants submit that the claims as amended describe the claimed polypeptide by reference to functional properties (immunologically identifiable by specific antibodies) sufficiently correlated to a known structure (SEQ ID NO:3), in accordance with the holding of the Federal Circuit in *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316 (Fed. Cir. 2002). Accordingly, Applicants request withdrawal of the rejection.

III. The claims are patentable over Cover et al.

Claims 40, 54, 58-65, 69-75, 79-86, and 90-101 have been rejected under 35 U.S.C. § 102(e), or, alternatively, 35 U.S.C. § 103 in view of Cover et al. (U.S. Patent No. 6,054,132). Applicants disagree. Preliminarily, Applicants note that claims 58-60, 69-71, 79-81, 90-92, and 97 have been canceled herein without prejudice.

Cover et al. describes the purification and direct sequencing of the amino-terminal 23 amino acids of the 87 kDa vacuolating toxin of *Helicobacter pylori* strain 60190, having toxic activity. Cover et al. does not describe a recombinantly produced *H. pylori* CT polypeptide comprising SEQ ID NO:3 or expressed from the nucleotide sequence of SEQ ID NO:2, or fragments thereof, which polypeptide comprises at least ten or fifteen contiguous amino acids, is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3 or with the polypeptide expressed from the nucleotide sequence of SEQ ID NO:2, and exhibits substantially no toxicity, or substantially reduced toxicity.

A. *The solicited claims are not inherently anticipated.*

It is asserted that the 23-amino acid fragment (SEQ ID NO:1) disclosed by Cover et al. is inherently nontoxic (*see* Office Action at page 7), thereby inherently anticipating claims 40, 54, 61-65, 72-75, 82-86, 93-96, and 98-101. Applicants disagree.

That a certain result or characteristic *may* occur or be present in the prior art is not sufficient to establish inherency of that result or characteristic. In relying upon a theory of inherency, the Examiner must provide a basis in fact and/or technical reasoning to support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art. *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990).

> To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. ***Inherency, however, may not be established by probabilities or possibilities.***

In re Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations omitted) (emphasis added).

It is asserted in the Office Action that the polypeptide fragments of Cover et al. are inherently non-toxic since only a portion of the CT molecule is responsible for toxicity:

> While it is remotely possible that Cover unwittingly isolated fragments which included the toxic portion of the molecule, it is much more likely that these fragments did not include the toxic portion or enough of the toxic region to be toxic. Accordingly, *the conclusion of inherency is founded on* ***the high probability*** *that Cover's fragments are non-toxic portions of the cytotoxin.*

Office Action at page 7. Applicants submit that the Examiner's reliance on probability is insufficient to establish that the polypeptide fragment of Cover et al. is inherently nontoxic.

Moreover, Applicants respectfully submit that Cover et al. does not teach that the polypeptides disclosed therein are immunologically identifiable by antibodies that react

specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3 or with the polypeptide expressed from the nucleotide sequence of SEQ ID NO:2, as required by the amended claims.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. *The solicited claims are not obvious in view of Cover et al.*

It is alternatively asserted that the production of nontoxic fragments of Cover et al.'s polypeptides would have been obvious in view of the disclosure of Cover et al. and statements made in the Del Giudice Declaration. Applicants disagree. Nonetheless, in order to advance prosecution of the application, Applicants have amended the claims to overcome the rejection. Applicants respectfully submit that Cover et al. neither teaches nor suggests that the polypeptides disclosed therein are immunologically identifiable by antibodies that specifically react with the polypeptide having the amino acid of SEQ ID NO:3 or with the polypeptide expressed from the nucleotide sequence of SEQ ID NO:2. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

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CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please contact the undersigned at 215-557-5908.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Respectfully submitted,

Date: April 1, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Please amend claims 40, 55, 63, 74, 76, 84, 95, and 99 as follows:

40. (Four times amended) A recombinant polypeptide comprising at least ten contiguous amino acids from SEQ ID NO:3, which polypeptide:

(i) is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3 [can induce the production of antibodies to *Helicobacter pylori* cytotoxin (CT) polypeptide] and

(ii) exhibits substantially no toxicity, or substantially reduced toxicity.

55. (Amended) The recombinant polypeptide of claim 40 or 54, said polypeptide further comprising a fragment [or a derivative] of a *Helicobacter pylori* CT polypeptide.

63. (Amended) A recombinant polypeptide expressed from at least 15 contiguous nucleotides of SEQ ID NO:2, wherein said polypeptide:

(i) is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3 [can induce the production of antibodies to *Helicobacter pylori* cytotoxin (CT) polypeptide] and

(ii) exhibits substantially no toxicity, or substantially reduced toxicity.

74. (Amended) An immunogenic, recombinant polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO:3, [and further] wherein said polypeptide exhibits substantially no toxicity or substantially reduced toxicity, and wherein said polypeptide is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3.

76. (Amended) The recombinant polypeptide of claims 74 or 75, said polypeptide comprising an immunogenic fragment [or an immunogenic derivative] of a *Helicobacter pylori* CT polypeptide.

84. (Twice Amended) An immunogenic, recombinant polypeptide comprising at least 5 contiguous amino acids expressed from at least 15 contiguous nucleotides of SEQ ID NO:2, wherein said polypeptide exhibits substantially no toxicity or substantially reduced toxicity and wherein said polypeptide is immunologically identifiable by antibodies that react specifically with the polypeptide expressed by the nucleotide sequence of SEQ ID NO:2 [can induce the production of antibodies to *Helicobacter pylori*].

95. (Amended) A recombinant polypeptide of a *Helicobacter pylori* cytotoxin, wherein:

(i) said cytotoxin causes the formulation of vacuoles in eukaryotic cells;

(ii) said recombinant polypeptide exhibits substantially no toxicity, or substantially reduced toxicity, and

(iii) said polypeptide is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3 [said recombinant polypeptide can induce the production of antibodies to a *Helicobacter pylori* cytotoxin].

99. (Twice Amended) A recombinant polypeptide of a *Helicobacter pylori* cytotoxin, wherein:

(i) said cytotoxin causes the formation of vacuoles in eukaryotic cells,

(ii) said recombinant polypeptide exhibits substantially no toxicity, or substantially reduced toxicity,

(iii) said recombinant polypeptide [can induce the production of antibodies to a *Helicobacter pylori* cytotoxin] is immunologically identifiable by antibodies that react specifically with the polypeptide having the amino acid sequence of SEQ ID NO:3, and

(iv) said polypeptide is expressed from at least 15 contiguous nucleotides from SEQ ID NO:2.

Please cancel claims 58-60, 69-71, 79-81, 90-92, and 97 without prejudice and without disclaimer of the subject matter contained therein.